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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

The amendment filed on April 22, 2009 has been received and entered. Claims 55, 60 and 89-91 have been amended. Claims 1-54, 63, 66, 68-70, 72-78, 80, 82, 84, 86, 88 and 92-102 have been canceled. No claims have been added.

Claim Rejections - 35 USC § 112, second paragraph

Claims 55-62, 64-65, 67, 71, 79, 81, 83, 85, 87, 89-91 and 103-105 are again rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This rejection has been discussed in the previous Office actions.

Similarly to the discussion in the previous Office action, although claims 55 and 60 have been amended, they are still confusing and ambiguous in their recitation of the claimed microfluidics system, and the structure of the claimed apparatus still cannot be understood, rendering the meaning of claims unclear. As previously discussed, it is not clear if the claimed device is a one-piece structure or a two-piece structure, and Applicants have not addressed this point. If the device is a two-piece structure, is the substrate the base (i.e., a modified microtiter plate) or is it the lid for the base or is it both?

As previously discussed and as noted by Applicants, in claim 55, the substrate comprises a measurement chamber and a raised aperture. The raised aperture comprises a tip, and the tip comprises a housing. The measurement chamber comprises a microchannel. But, the relationship of these parts is unclear, particularly the relationship of the aperture, the tip, the substrate and the measurement chamber. As previously discussed, it is not clear if the substrate is a one-piece device (a molded plate having apertures or tips, an internal or external plumbing system and wells or reservoirs) or a two-piece device (with the apertures and tips in the upper part and the plumbing and wells in the lower part). Additionally, the microchannel

need not be connected to anything but the measuring chamber, and the measuring chamber need not be connected to anything. Thus, the structure, how its parts fit together, and how the claimed apparatus is used are unclear. Claim 60 recites the same apparatus as claim 55 with the change that the aperture is a plurality of solid electrode tips. Applicants have added the limitation that the substrate has a microchannel with an inlet and an outlet that opens into the measuring chamber, but this limitation does not serve to clarify how any of the structures are arranged in the device as a whole.

In their Response, as in their previous Response, Applicants refer to certain drawings and indicate that these structures are encompassed by the claims. But the claims are much broader than the embodiments shown in the drawings. Clear and definite structures must still be recited in the claims. As previously discussed, specific reference to specific figures as a claim requirement would clarify the relationship of the components. This is commonly done in device claims. Typically when this is done, the figures provide numbered parts for reference. Because the instant figures lack reference characters, as does the specification, new drawings and amendments to the specification might be needed. It is noted that the rejection under 103 below is based in part on a broad interpretation of the device. Clarification and appropriate correction are again required.

Amended claim 90 is somewhat clearer than its previous version, as the limitation of "translating the cells across the microchannels" has been deleted. But the limitation of "scanning a cell across the aqueous streams from the microchannels" is still unclear and confusing. Applicants refer to descriptions of Figs. 18A-F, which recite that electrode-contacted cells in the microchannel outlets are scanned, or that the outlets are scanned relative to stationary electrode-contacted cells. But, these features are not recited in the claim. The claim may mean that the microfluidics system further comprises a scanning apparatus that scans cells

or scans for cells by scanning across the width of one or more outlet channels. It is not clear, however, if the scanning is meant to create an image of the cell or to detect whether or not a cell is present at a particular point in time. Clarification and appropriate correction are again required.

Claim Rejections - 35 USC § 103

Claims 55-62, 64-65, 67, 71, 79, 81, 83, 85, 87, 89-91 and 103-105 are again rejected under 35 U.S.C. 103(a) as being unpatentable over Maher et al. (US 2002/0025568 A1) and He et al. (US 2003/0049862 A1) in view of Peeters (US 6,123,819) and Hamill et al. ("Improved patch-clamp techniques for high-resolution current recording from cells and cell-free membrane patches," Pflügers Archiv 391:85-100, 1981). This rejection has been discussed in the previous Office actions.

As discussed in the previous Office action, Maher et al. disclose an apparatus for carrying out electrical measurements on cells. The apparatus comprises a substrate comprising an array of measurement chambers (a microtiter plate) that contain cells. The apparatus comprises an array of microelectrodes that match the wells in the microtiter plate and that are arranged in a lid or cover. The microelectrodes may be solid (i.e., have solid tips) or fluid filled (patch clamp electrodes). Hamill et al. were cited for their disclosure of the structure and properties of patch clamp electrodes. The apparatus of Maher et al. is part of a computer-controlled system that operates the electrical, mechanical and optical aspects of the apparatus, as it controls the activity of the electrodes, movement of the microtiter plate, spectroscopic readings of the wells in the microtiter plate, and data collection and analysis. The electrodes are compatible with microfluidics equipment (see paragraphs 197, 198, 202 and 205-208). Maher et al. do not disclose that the measurement chambers have microchannels.

He et al. disclose a microfluidics system, in which the microfluidics plumbing is incorporated into the lid for a standard microtiter plate, thereby providing the measurement chambers with microchannels. See paragraphs 6-12 and 37-45. The measurement chambers are circular and the microchannels may be radially disposed with outlets in the chambers (see paragraph 39). The system comprises a pressure control device for controlling the positive and negative pressures to the microchannels, which fills and empties the measurement chambers, allowing assays to be performed and the chambers to be washed (see paragraph 49).

The claimed microfluidics system is the apparatus of Maher et al. in which the microtiter plate lid has been modified with the microfluidics plumbing of He et al. It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the microtiter plate of Maher et al. with the microfluidics plumbing for microtiter plate lids of He et al., because He et al. disclose that this modification transforms the apparatus into high-throughput apparatus, using standard industry equipment, for carrying out the most common types of automated assays used in the biotechnology and pharmaceutical industries, biochemical and genomics assays. Microfluidics chips, by comparison, require specialized custom equipment and have much lower throughput, i.e., they perform far fewer assays in the same amount of time (see paragraphs 6-7).

Regarding the computer-controlled equipment for manipulating the microfluidics system (claims 79, 81-83 and 87-91), as previously discussed, Peeters discloses a microfluidics system comprising a nanoelectrode array on a substrate in a measuring chamber that holds fluids. The array and the chamber are connected to a microfluidics system for the delivery and removal of materials to and from the array via microchannels. The array is connected to a microcontroller or microprocessor, which analyzes signals from the microelectrodes and controls the microfluidics system. The pressure in the microchannels is controlled by an external micro-

pump (see Figs. 1-3 and 5; col. 3, lines 21-35; and col. 8, line 38, to col. 9, line 7). Scanning of the nanoelectrode array in the x-y plane at specific positions is computer-controlled and very precise, similar to scanning a DNA chip, and scanning may be performed with a laser. Thus, the laser can scan a cell structure such as protein on the array relative to a microchannel outlet when the chip array of Figs. 1-3 is used in one of the chambers in Fig. 5. Signals from the electrodes can be amplified via transistors (see col. 10, lines 20-30; and col. 10, line 41, to col. 11, line 6). It would have been obvious to one of ordinary skill in the art at the time of the invention to use the computer-controlled equipment of Peeters with apparatus of Maher et al. (modified with the plumbing of He et al.), because, as noted above, Maher et al. disclose that their apparatus is designed for use with computer-controlled equipment. Peeters discloses the same computer-controlled equipment but is more explicit about the specific tasks and operations that the equipment performs.

In their Response, Applicants assert that Maher et al. do not teach the limitation of the substrate comprising a microchannel with an inlet and an outlet that opens into the measurement chamber, that He et al. do not teach all of the limitations recited in claims 55 and 60, and that it would not be possible to use the plumbing of He et al. in the apparatus of Maher et al. to arrive at the claimed invention. In reply, the rejection is one of obviousness over the combination of the cited references, not one of anticipation by Maher et al. or He et al. Motivation to combine the references is provided above and was discussed in the previous Office action, i.e., that it would have been obvious to modify the apparatus of Maher et al. with the microfluidics plumbing of He et al. in order to convert this device into a high-throughput assay device or one suited for automated assays. The artisan of ordinary skill would have known that a microtiter-plate-based device in which each reagent or waste solution must added to or removed from each well by hand is of very limited use. Applicants have not explained why

the artisan of ordinary skill would not have been able to make this modification. This modified construction would have been routine for one of ordinary skill in the art, and he would have had every expectation of success in making this modification to arrive at the claimed invention.

Regarding Peeters, it is clear in the previous Office actions that this reference was cited for its teachings of the hardware and software needed to manipulate, move and scan a micro-scale assay device, particularly one with a planar shape. It is clear that this reference was not cited for teaching patch clamp electrodes or the apparatus of claims 55 and 60. As a result, Applicants' argument that Peeters does not render the claimed invention obvious is not persuasive.

In view of the foregoing, the rejection of record is maintained.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rosanne Kosson whose telephone number is (571)272-2923. The examiner can normally be reached on Monday-Friday, 8:30-6:00, alternate Mondays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nashaat Nashed can be reached on 571-272-0934. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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